WEST Search History

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DATE: Wednesday, October 27, 2004

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	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L13	L12 and l9	7
☐	L12	MUNDY-GREGORY-$.in.	55
☐	L11	L9 and l8	0
☐	L10	L9 and 38	5
☐	L9	YONEDA-TOSHIYUKI.in.	52
☐	L8	MUNDY-GREGORY.in.	3
☐	L7	L1 same (multiple adj myeloma)	22
☐	L6	L5 .clm.	16
☐	L5	L1 same ((multiple adj myeloma) or mm)	342
☐	L4	L2 same (myeloma or mm)	20
☐	L3	L2 same myeloma or mm	1221704
☐	L2	L1 adj (anti or antibod$)	183
☐	L1	CD49$ or (alpha adj 4 adj beta adj 1) or (alpha adj 4) or alpha4 or (vla adj 4) or vla4 or (very late antigen adj 4)	8545

END OF SEARCH HISTORY

h e b b cg b chh e bb f c e h

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=> d his

     (FILE 'HOME' ENTERED AT 11:02:08 ON 27 OCT 2004)

     FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
     COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, MEDICONF,
     OCEAN, PAPERCHEM2, PASCAL, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT,
     ADISNEWS, ANABSTR, ANTE, AQUALINE, BIOBUSINESS, ...' ENTERED AT 11:05:04
     ON 27 OCT 2004
L1       159143 S (CD49D? OR CD29)OR (ALPHA (A) 4 (A) BETA ) OR (ALPHA (A) 4) O
L2         4816 S L1 (A) (ANTI OR ANTIBOD?)
L3            6 S L2 (W) (MULTIPLE MYELOMA)
L4            6 DUP REM L3 (0 DUPLICATES REMOVED)
L5           32 S L2 (S) (MULTIPLE MYELOMA)
L6           18 DUP REM L5 (14 DUPLICATES REMOVED)
                E YONEDA TOSHIYUKI?/AU
L7          380 S E2
                E MUNDY GREGORY?/AU
L8            4 S E1 OR E2
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L6 ANSWER 18 OF 18 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1992:22332064 BIOTECHNO
TITLE: Characterization of adhesion molecules on human myeloma cell lines
AUTHOR: Uchiyama H.; Barut B.A.; Chauhan D.; Cannistra S.A.; Anderson K.C.
CORPORATE SOURCE: Division of Tumor Immunology, Dana-Farber Cancer Institute, 44 Binney St,Boston, MA 02115, United States.
SOURCE: Blood, (1992), 80/9 (2306-2314)
CODEN: BLOOAW ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In **multiple myeloma**, malignant plasma cells are localized in marrow and rarely circulate in peripheral blood. To investigate the role of adhesion proteins in this process, we determined the expression and function of adhesion molecules on cell lines derived from patients with myeloma. The U266, ARH-77, IM-9, and HS-Sultan cell lines strongly expressed β1 and α4 integrins (89% to 98% positive), confirming that VLA-4 is the principal integrin on these cell lines. The U266 and IM-9 cell lines also expressed α.sub.3 integrin on 15% to 20% cells. In contrast, all lines lacked cell surface α2, α5, and α6 integrin expression (<5% positive). These cell lines adhered to fibronectin (20% to 40% specific binding), without significant binding to either collagen or laminin. Adhesion of these cell lines to fibronectin was partially blocked with either anti-β1 integrin monoclonal antibody (MoAb) (75% inhibition), **anti-.alpha.4** integrin MoAb (75% inhibition), or RGD peptide (50% inhibition), but was unaffected by anti-αvβ3 or anti-αIIbβ3 MoAbs. Moreover, the combination of anti-β1 plus RGD peptide or **anti-.alpha.4** plus RGD peptide inhibited binding to fibronectin by 80% and 95%, respectively. Finally, pretreatment and coculture of the IM-9 cell line with interleukin-6 (IL-6) resulted in a 52% decrease in specific binding to fibronectin (30% ± 6% to 15% ± 6%; P = .001), associated with a decrease in the number of cells expressing VLA-4 and a decrease in intensity of VLA-4 expression. These data suggest that myeloma cells adhere to fibronectin through VLA-4 as well as through RGD-dependent mechanisms, and that this binding can be downregulated by IL-6. Future studies of binding of both myeloma cell lines and freshly isolated tumor cells to extracellular matrix proteins and to marrow stroma may enhance our understanding of localization and trafficking of cells within the bone marrow microenvironment.

AB In **multiple myeloma**, malignant plasma cells are localized in marrow and rarely circulate in peripheral blood. To investigate the role of adhesion proteins. . . laminin. Adhesion of these cell lines to fibronectin was partially blocked with either anti-β1 integrin monoclonal antibody (MoAb) (75% inhibition), **anti-.alpha.4** integrin MoAb (75% inhibition), or RGD peptide (50% inhibition), but was unaffected by anti-αvβ3 or anti- αIIbβ3 MoAbs. Moreover, the combination of anti-β1 plus RGD peptide or **anti-.alpha.4** plus RGD peptide inhibited binding to fibronectin by 80% and 95%, respectively. Finally, pretreatment and coculture of the IM-9 cell. . .

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L6 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:807992 CAPLUS

TITLE: **Anti-.alpha.4** integrin antibody suppresses the development of **multiple myeloma** and associated osteoclastic osteolysis

AUTHOR(S): Mori, Yoshihisa; Shimizu, Nobuaki; Dallas, Mark; Niewolna, Maryla; Story, Beryl; Williams, Paul J.; Mundy, Gregory R.; Yoneda, Toshiyuki

CORPORATE SOURCE: Division of Endocrinology, the Department of Medicine, The University of Texas Health Science Center at San Antonio, TX, USA

SOURCE: Blood (2004), 104(7), 2149-2154
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Supporting roles of stromal cells in preferential colonization of myeloma cells in bone marrow and development of associated osteoclastic osteolysis through cell-cell interactions have been indicated. Here we examined the effects of a monoclonal antibody to α4 integrin (anti-α4 Ab) that disrupts myeloma cell-stromal cell interactions mediated via α4β1 integrin and vascular cell adhesion mol.-1 (VCAM-1) on myeloma cell growth in bone marrow and accompanying osteolysis. The anti-α4 Ab decreased VCAM-1-stimulated 5TGM1/luc cell growth in culture. The 5TGM1 murine myeloma cells stably transfected with the firefly luciferase (5TGM1/luc) were inoculated from tail vein in bg/xid/nd mice. Preventative administration of the anti-α4 Ab suppressed the elevation of serum IgG2b levels, decreased 5TGM1/luc tumor burden with increased apoptosis in bone and spleen, reduced bone destruction with diminished number of osteoclasts, and prolonged survival of 5TGM1/luc-bearing mice. In contrast, therapeutic administration of the antibody failed to show these effects. However, therapeutic administration of the antibody combined with melphalan significantly suppressed serum IgG2b levels and tumor burden in bone. Our results suggest that the interactions with stromal cells via α4β1/VCAM-1 are critical to the development of myeloma and associated osteolysis and that disruption of these interactions using anti-α4 Ab is a potential therapeutic approach for myeloma.

TI **Anti-.alpha.4** integrin antibody suppresses the development of **multiple myeloma** and associated osteoclastic osteolysis